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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/823,998	04/14/2004	Julia Billiard	2004658-0047 (AM101291)	7072

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Patent Department
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EXAMINER	
XIE, XIAOZHEN	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
08/08/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/823,998	BILLIARD ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-27 and 93-96* is/are pending in the application.

4a) Of the above claim(s) *21,22,24,26,93 and 95* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,23,25,27,94 and 96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 April 2004 and 08 June 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendments of the drawings, the specification, and the claims filed 8 June 2007 have been entered.

Claims 1-19 and 28-92 have been cancelled. Claims 93-96 have been added. Claims 20-27 and 93-96 are pending. Claims 21, 22 and 24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. Applicant elected species of: Ror2 for a Ror and Ror autophosphorylation for a Ror activity, in the reply filed on 29 January 2007. Therefore claims 20, 23, 25-27 and 93-96 are under examination to the extent they read on the elected species. Claims 20, 23, 25, 27, 94 and 96 read on the elected species.

Drawings

The objection to the drawings as being not legible (Figures 13, 15 and 16) is withdrawn in response to Applicant's submission of the replacement of the drawings.

Specification

The objection to the abstract for containing statements that are not related to the content of the invention is withdrawn in response to Applicant's amendment of the abstract.

Claim Rejections Maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20 and 23 remain rejected under 35 U.S.C. 102(b) as being anticipated by Clary (WO 98/457080) for reasons set forth in the previous office action.

Applicant argues that Clary does not teach that the identified agent is a "bone-related agent". Applicant argues that although Clary in general describes a method of identifying modulators of RPTK activity in a cell, it does not specifically point out Ror family members, and that Ror1 and Ror2 are merely included in a laundry list of receptor tyrosine kinases in Clary. Applicant argues that Clary does not teach or suggest any such connection between Ror family members and bone metabolism.

Applicants' argument has been fully considered but has not been found to be persuasive.

The method claimed in the instant invention comprises two steps: a) combining an agent with a Ror molecule; and b) detecting an effect of said agent on Ror activity (i.e., a decrease or an increase in Ror activity). Clary teaches a method of identifying one or more compounds that modulate the function of a RPTK (such as Ror2) in a cell (pp. 16, lines 30-32, pp. 19, lines 9-14). Clary

teaches that the method comprises the steps of: (a) transfecting a nucleic acid encoding a chimera comprising an extracellular region and an intracellular region, wherein the intracellular region is from the RPTK (note that the specification defines a Ror molecule as Ror polypeptides, Ror peptides, fragments, variants, and mutants thereof, as well as nucleic acids encoding same (pp. 19, lines 11-17)); (b) contacting the cells with one or more compounds; (c) contacting the cells with an antibody, where the antibody has specific binding affinity to the extracellular region; and (d) monitoring the effect on the cell to identify compounds that modulate the function of the RPTK (pp. 16, lines 32 through pp. 17, line 9). Even though Clary is silent on any connection between Ror family members and bone metabolism, it would have been inherent that the identified agent is a "bone-related agent" because Clary teaches the same method steps as the claimed invention.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 25 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Clary, in view of Oishi et al.

Applicant argues that neither reference teaches the connection between Ror and bone metabolism, and that the two references even in combination

cannot render obvious the claimed invention because neither reference teaches that the modulators of Ror are bone-related agents.

Applicants' argument has been fully considered but has not been found to be persuasive.

As set forth above, even though Clary is silent on any connection between Ror family members and bone metabolism, it would have been inherent that the identified agent is a "bone-related agent", because Clary teaches the same method steps as the claimed invention. Clary, however, does not teach that Ror2 has autophosphorylation activity. Oishi teaches that both Ror1 and Ror2 tyrosine kinases exhibit autophosphorylation activities (pp. 47, right column, last paragraph). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Clary, with those of Oishi, to measure Ror2 autophosphorylation in a screening method that requires determining the effect of a compound on Ror2 activity.

New Grounds of Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 94 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed does not provide support for the invention as now claimed: "wherein the Ror molecule is wild type Ror2 polypeptide". Applicant's amendment, filed 8 June 2007, asserts that no new matter has been added and directs support for the newly added claims at various sections of the instant specification (pp. 86, lines 3-25). However, the instant specification as filed does not provide sufficient written description for the limitation of "a wild type Ror2". This is a new matter rejection.

Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 23, 25, 27, 94 and 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Godowski et al. (U. S. Patent No: 5,766,863, issued on 16 June 1998), in view of Oishi et al. (Genes to Cells, 1999, 4:41-56).

The instant claims are dawn to a method of screening for agents, comprising: a) combining an agent with a Ror molecule; and b) detecting an

effect of said agent on Ror activity; wherein detection of a decrease or an increase in Ror activity is indicative of an agent being a bone-relate agent (claim 20); wherein Ror activity is Ror autophosphorylation (claim 25), and Ror molecule is Ror2 (claim 23, 27), wild type Ror2 (claim 94), or FLAG-tagged Ror2 (claim 96).

The '863 patent teaches an assay for measuring activation (i.e., autophosphorylation) of a tyrosine kinase receptor of interest. The '863 patent teaches that the method comprises the steps of: a) coating the first solid phase (e.g., a well of an assay plate) with a substantially homogeneous population of cells, wherein the cells have an endogenous tyrosine kinase receptor (wild type) presented in the cell membrane, or the cells have been transformed with DNA encoding a tyrosine kinase receptor ("receptor construct"); b) an analyte is then added to the wells such that the tyrosine kinase receptor is exposed to (or contacted with) the analyte (the term "analyte" refers to a compound or composition to be studied for its ability to activate or prevent activation of the tyrosine kinase receptor of interest (column 12, lines 24-26); and c) following exposure to the analyte, the cells are solubilized and subject to measuring autophosphorylation for the tyrosine kinase receptor of interest (column 4, line 19 through column 6, line 6). The '863 patent teaches that the receptor construct comprises a fusion of a kinase receptor and a FLAG polypeptide (column 4, line 50-51). The '863 patent teaches that the assay is useful for screening molecules which activate or antagonize the tyrosine kinase receptor of interest (column 25, lines 13-21).

The '863 patent, however, does not teach Ror2.

Oishi teaches that both Ror1 and Ror2 are receptor tyrosine kinases that exhibit autophosphorylation activities (see Abstract and pp. 47, right column, last paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the '863 patent, with those of Oishi, to measure Ror2 autophosphorylation in a screening method to identify agents that modulate Ror2 activity. One of ordinary skill in the art would have been motivated to combine the teachings, because the '863 patent teaches a screening method for identifying molecules which activate or antagonize a tyrosine kinase receptor of interest by measuring effects of the agents on the RTK autophosphorylation, and Oishi teaches that Ror1 and Ror2 are tyrosine kinase receptors and exhibit autophosphorylation activities. Therefore, the teachings provide a reasonable expectation of successfully screening for the agents.

Conclusion

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
July 26, 2007

Eileen B. O'Hara

EILEEN B O'HARA
PRIMARY EXAMINER